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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,142	03/31/2000	JEAN MARTINEZ	427.034	1834

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CHARLES A MUSERLIAN
BIERMAN MUSERLIAN AND LUCAS
600 THIRD AVENUE
NEW YORK, NY 10016

EXAMINER	
SAKELARIS, SALLY A	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 08/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,142	MARTINEZ ET AL.	
	Examiner	Art Unit	
	Sally A Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-29 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-29 and 33* is/are rejected.

7)☒ Claim(s) *27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: SEQ SRCH STN RESULTS Attached to Action

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 3/05/2004 and 6/8/2004 have been entered.

This action is written in response to applicant's correspondence submitted 3/05/2004. Claims 26, 27, and 29 have been amended, claims 1-25 and 30-32 have been canceled, and new claim 33 has been added. Claims 26-29 and 33 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is non-final.**

Claim Status

Specifically, applicant should note that their amendment to claim 27 is improper. Applicant's alteration of the claim language without properly identifying their changes to claim 27 is misleading to the examiner. Claim 27 is void of any markings that reveal that the recitation of "hydrogen" is being newly added to the claim. It would appear as if the recitation of "hydrogen" was present in an earlier version of the claims and as such, had been examined previously. However, it appears to be presented for the first time in this after final amendment of

3/5/2004. In an attempt to provide compact prosecution to the applicant though, the examainer will still examine the claims as they are presently written.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With respect to claim 29, claim 29 is drawn broadly to a single-stranded oligonucleotide OZ consisting of 15 to 39 nucleotides and capable of hybridizing under mild or stringent conditions with a consensus signal characteristic of amidated polypeptide hormones with the sequence having the formula Z1-Z2-Z3-Z4-Z5-Z6-Z7 wherein, among other things, Z1 and Z7 are nucleotide sequences of 1 to 12 nucleotides or are hydrogens, and Z4 and Z5 are two trinucleotides which code for any two amino acids. The specification indicates that the nucleotides of the sequence, Z1-Z2-Z3-Z4-Z5-Z6-Z7, are essential to the operation and function of the claimed invention. A review of the language of the claims indicates that the claims are drawn to a genus, i.e., any nucleic acid that minimally contains these aforementioned sequences in addition to any full length gene which contains the sequence, any splice variants, or cDNAs. The disclosure of a single disclosed species may provide an adequate written description of a

genus when the species disclosed is representative of the genus. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. The present claims encompass full-length genes, cDNAs and other oligonucleotides whose exact composition are not further described. There is substantial variability among the species of DNAs encompassed within the scope of claim 29's 15-39 nucleotides of their "OZ" sequences, wherein some positions can be any amino acid and in still others, the nucleotides need only to hybridize under mild conditions with a consensus signal with the sequence, Z1-Z2-Z3-Z4-Z5-Z6-Z7, encompass a great deal more than just the

enumerated sequences listed. The specification describes sequences OY and OZ as oligos which hybridize with a DNA sample and identifies a sequence in the sample, of at least one non-amidified precursor of peptides with an optional amidated C-terminal end position. Further, the specification provides only that this claimed "hybridization" takes place if two oligonucleotides have substantially complementary nucleotide sequences, and that they can combine over their length by establishing bonds(Pg.6). The specification does not limit the amount of sequences capable of hybridizing, by including an amount of similarity across a certain length that is necessary for hybridizing. Also, the specification states that certain OY or OZ nucleotides can encode a wide variety of amino acids with differing lengths, not to mention that certain amino acids may or may not even be present. Furthermore, the specification does not teach all of the possible structures that could exist for the OY and OZ oligonucleotides considering the many different definitions of "mild conditions" that exist. The specification also does not teach how the very different possible structures claimed, share similar functions. The claims are written such that they encompass sequences of any length and composition for certain amino acid positions which only minimally contain the few, requisite trinucleotide sequences and amino acids as specified in claim 29, but, could include genes and/or regulatory domains which have not been described and of which applicant does not appear to have been in possession.

Weighing all factors, 1) partial structure of the DNAs of an oligonucleotide consisting of 15-39 nucleotides of their "OZ" sequences, wherein some positions can be any amino acid and in still others, the nucleotides need only to "hybridize" under mild conditions with a consensus signal with the sequence, Z1-Z2-Z3-Z4-Z5-Z6-Z7, encompass a great deal more than just the enumerated sequences listed, 2) the breadth of the claim as reading on genes yet to be discovered

in addition to numerous splice variants and cDNAs, 3) the lack of correlation between the structure and the function of the genes and/or splice variants; in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of oligonucleotides consisting of 15-39(Claim 29) nucleotides of their "OZ" sequence, wherein some positions can be any amino acid and in still others, the nucleotides need only to "hybridize"(in the very broadly defined manner of the specification) under mild conditions with a consensus signal with the sequence, Z1-Z2-Z3-Z4-Z5-Z6-Z7.

Response to Arguments:

Applicant's arguments filed 3/05/2004 have been fully considered but they are not persuasive. Applicant's amendment including the term "consisting of" is noted, but does not remedy the present claims' lack of written description. The applicant does not provide a single disclosed species that may provide an adequate written description of a genus when the species disclosed is representative of the genus. The genus is very large considering the many "mild conditions" that could be enlisted to allow for hybridization of hypothetically very different sequences.

2. Claims 26-29 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the

claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the limitation of hydrogen newly added in claims 26, 27, 29 and 33 appears to represent new matter. In addition the limitation of "with the exception of CGACACUCCACCAUA" in claim 26 also appears to represent new matter. No specific basis for either of these limitations was identified in applicant's disclosure, nor did a review of the specification by the examiner find any basis for the limitation. Specifically, the exclusion proviso in which "all others" are distinguished is not found in the specification. As noted by MPEP 2173.05(i),

"Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement."

Since no basis has been identified, the claims are rejected as incorporating new matter.

Response to Arguments:

Applicant did not respond make any arguments concerning this maintained grounds of rejection, nor did they amend their claims to remedy the rejection, applicant is encouraged to make note this rejection.

THE FOLLOWING ARE NEW REJECTIONS

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 26-29 and 33 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a single stranded oligonucleotide OY and OZ consisting of 9 to 42 and 15-39 nucleotides respectively that is used in a method for identifying the non-amidified precursor of a peptide having an amidated C-terminal end.

Credible Utility

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the proteins. The cited utilities identified in the specification is the identification of the mRNA which codes for precursors of amidated polypeptide hormones and to the identification of new amidated polypeptide hormones. These utilities are credible.

Upon identification of credible utilities, the next issue is whether there are any well established utilities for the protein. No well established utilities for this single stranded oligonucleotide OY and OZ consisting of 9 to 42 and 15 to 39 nucleotides are identified in either the specification or in the cited prior art.

Substantial utility

Given the absence of a well established utility, the next issue is whether substantial utilities are disclosed in the specification. Here, there is no evidence (in the form of published prior art) which supports a substantial utility. While the OY sequence of claim 28 is not known in the prior art, the remaining OY and OZ sequences are well known but have utilities that range from characterization of RNA viral and subviral pathogens to being primers from the iagA and

iagB genes for the detection of Salmonella. Further, the specification identifies no utility which is substantial regarding this sequence.

As noted in the utility guidelines, methods of treating unspecified diseases, basic research on a product to identify properties, intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline training materials). The claim to a single stranded oligonucleotide OY and OZ consisting of 9 to 42 and 15-39 nucleotides that is used in a method for identifying the non-amidified precursor of a peptide having an amidated C-terminal end where there is no particular phenotype associated with the detection claimed, does not support a substantial utility for an oligonucleotide with a myriad of known and unknown functions. Further, where no association has been made between oligonucleotide and the detection of any particular phenotype or disease state, the specification does not support a substantial utility for these oligonucleotides, OY and OZ with unknown function which is not associated with any disease.

Specific Utility

In the current case, there is no specific utility because the use of the claimed nucleic acid is not particular to the sequence being claimed. Any asserted utility would be applicable to the general class that could identify mRNA which codes for precursors of amidated polypeptide hormones. Any partial nucleic acid prepared from any cDNA may be used as a probe in the preparation and or identification of a full-length cDNA. As the utility guideline training materials note on page 5-6, "Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed". Here, there is no disclosure of any condition which can be

diagnosed and hence, no specific utility. A starting material that can only be used to produce a final product does not have a substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case the amidated polypeptide hormone mRNA that is to be identified as final products resulting from processes involving the claimed oligonucleotides has no identified specific and substantial utilities. The research contemplated by applicants to allow pharmacological study of active substances having a fundamental physiological roll in the mammalian organisms, does not constitute a specific and substantial utility. Identifying and studying the properties of the amidated hormone itself does not define a "real world" context of use. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the oligonucleotide compounds such that another non-asserted utility would be well established for the compounds.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 26-29 and 33 are rejected under 35 U.S.C. 112, first paragraph, as the specification's lack of utility leaves the disclosure void also of any direction of how to use the presently claimed invention. As such, Claims 26-29 and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claims 26-29 and 33 are drawn to a single stranded oligonucleotide OY and OZ consisting of 9 to 42 and 15-39 nucleotides that is used in a method for identifying the non-amidified precursor of a peptide having an amidated C-terminal end. However, as will be further discussed, there is no support in the specification and prior art for the oligonucleotides or their uses in any method. The invention is an class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

The specification recites several possible single stranded oligonucleotide OY and OZ consisting of 9 to 42 and 15-39 nucleotides that is used in a method for identifying the non-amidified precursor of a peptide having an amidated C-terminal end. The specification discloses that all of these can be used in a pharmacological study of active substances having a fundamental physiological roll in the mammalian organisms(Pg. 3). However, there is no

evidence that said method even if it had a utility, would be operable using the disclosed oligonucleotides.

There is a great deal of unpredictability in pharmacological study of active substances having a fundamental physiological roll in the mammalian organisms. Especially since the prior art teach many variant uses for these same oligonucleotides, such as for probes for alpha satellite DNA variants that can distinguish homologous chromosomes by FISH(O'Keefe et al.), sequences of enhanced folding regions of hairpin ribozymes(Komatsu et al.), and as DR-DR5 elements that can function as RAREs in the RARBeta2 promoter(Sanguedolce et al.)

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied to apply this technology to a pharmacological study of active substances having a fundamental physiological roll in the mammalian organisms. For only to identify mRNA which codes for precursors of amidated polypeptide hormones, one must also consider (a) the ability of the oligonucleotide to specifically bind the target gene; (b) formation of a stable complex between the oligonucleotide and the target gene (note that modification of the oligonucleotide may interfere with its ability to form stable hydrogen bonds, whereas in pharmacological studies one must further consider; (c) uptake of the oligonucleotide by the cell; (d) solubility of the oligonucleotide of the cell, and other such constraints. For example, with regard to the specificity issue, the OY would hybridize to 1108 sequences identified in Registry file while OZ would hybridize to 199,211 sequences of the Registry file. The time table necessary to achieve efficacious administration or identification of effective oligonucleotides, effective temperatures and pH conditions would require a very large quantity of experimentation for in vitro and in-vivo applications. This would require years

of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Working Examples

The specification has no working examples of pharmacological study of active substances having a fundamental physiological roll in the mammalian organisms or for the identification of mRNA which codes for precursors of amidated polypeptide hormones

Guidance in the Specification.

The specification provides no evidence that the disclosed oligonucleotides would be able to have any impact in the identification of mRNA which codes for precursors of amidated polypeptide hormones, let alone any pharmacological study of active substances having a fundamental physiological roll in the mammalian organisms. The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention. The specification merely discloses that these highly variable sequences could be used as probes to find any sequence really without specificity to precursors of amidated polypeptide hormones. Even if, arguendo, the oligonucleotide complex could be used to specifically identify precursors of amidated polypeptide hormones, there is no support for how this could alter or affect any phenotype whatsoever. There is no support for how any pharmacological study of active substances having a fundamental physiological roll in the mammalian organisms could be performed and to what end it would be performed.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the oligomers ability to identify precursors of amidated polypeptide hormones depends upon numerous known and unknown parameters such as the nucleotides present in the reaction, the hybridization conditions, i.e. stringency required, potential secondary structure, and oligonucleotide length the factor of unpredictability weighs heavily in favor of undue experimentation. Further, the prior art and the specification provides insufficient guidance to overcome the art recognized problems in the use of such highly diverse oligonucleotides in pharmacological study of active substances having a fundamental physiological roll in the mammalian organisms as claimed. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 26, 27, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Komatsu et al.(Biochemistry (1996), 35(30), 9815-9820).

Komatsu et al. teach sequences of hairpin ribozymes in Figure 1 that are single stranded oligonucleotide OY consisting of 9 to 42 nucleotides wherein Y1 is a nucleotide, Y2 is a trinucleotide which encodes for Gly, Y3 is a nucleotide coding for Arg and Y5 is a nucleotide sequence, Y6-Y7-Y8-Y9 wherein Y6 is a trinucleotide which codes for Ser, Y7 is a trinucleotide which codes for Ala, Y8 is a trinucleotide which codes for Glu and Y9 is absent. Please see attached alignment of OY and the sequence of Komatsu et al. It should further be noted that also inherent in this teaching is that of the oligonucleotide above wherein Y1 and Y9 are hydrogen. In solution, hydrogen would be expected to totally surround each of the oligos and would comprise the hydrogen bonding between the two strands when hybridized. But also the 3' end of the oligo would have a hydrogen present belonging to the exposed hydroxl group, while on the 5' end, depending on the exact nucleotide present(ACTor G) the hydrogen would be present in the form of an amino group or a methyl group at that end of the individual nucleotides.

6. Claims 26, 27, and 33 are also rejected under 35 U.S.C. 102(b) as being anticipated by Sanguedolce et al.(EMBO Journal (1997), 16(10), 2861-2873).

Sanguedolce et al. teach sequences of DR1-DR5 elements that can function as RAREs in the RARBeta2 promoter in Figure 1 that are single stranded oligonucleotide OY consisting of 9 to 42 nucleotides wherein Y1 is a nucleotide, Y2 is a trinucleotide which encodes for Gly, Y3 is a nucleotide coding for Arg and Y5 is a nucleotide sequence, Y6-Y7-Y8-Y9 wherein Y6 is a trinucleotide which codes for Ser, Y7 is a trinucleotide which codes for Ala, Y8 is a trinucleotide

which codes for Glu and Y9 is absent. Please see attached alignment of OY and the sequence of Komatsu et al. It should further be noted that also inherent in this teaching is that of the oligonucleotide above wherein Y1 and Y9 are hydrogen. In the case of Y2 and Y8, both adjacent to Y1 and Y9, both positions would include the presence of at least one hydrogen. In solution, hydrogen would be expected to totally surround each of the oligos and also comprise the hydrogen bonding between the two strands when hybridized. But also the 3' end of the oligo would have a hydrogen present belonging to the exposed hydroxl group, while on the 5' end, depending on the exact nucleotide present(ACTor G) the hydrogen would be present in the form of an amino group or a methyl group at that end of the individual nucleotides.

7. Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by O'Keefe et al(Human Molecular Genetics (1996), 5(11), 1793-1799.

O'Keefe et al. teach in their Figure 1, 17 alphoid variant probes and an alpha consensus sequence having the sequence of single-stranded oligonucleotide OZ consisting of 15 to 39 nucleotides that is able to hybridizes under mild or stringent conditions with a consensus signal characteristic of amidated polypeptide hormones with the sequence having the formula Z1-Z2-Z3-Z4-Z5-Z6-Z7 wherein Z1is a nucleotide, Z2 and Z3 are two trinucleotides which code for Leu, Z4 and Z5 are two trinucleotides which code for any two amino acids, Z6 is a trinucleotide which codes for Leu and Z7 is a nucleotide. Please see attached alignment of OZ and O'Keefe's sequence of Figure 1.

8. Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by Kasparkova et al.(Biochemistry 1996, 35, 16705-16713).

Kasparkova et al. teach in their Figure 1, the sequences of the synthetic oligodeoxyribonucleotides used in their study of site-specific d(GpG) intrastrand cross-links formed by dinuclear platinum complexes. Specifically, Figure 1's 20 nt sequence(3rd down) anticipates the oligonucleotide OZ consisting of 15 to 39 nucleotides that is able to hybridizes under mild or stringent conditions with a consensus signal characteristic of amidated polypeptide hormones with the sequence having the formula Z1-Z2-Z3-Z4-Z5-Z6-Z7 wherein Z1is a nucleotide, Z2 and Z3 are two trinucleotides which code for Leu, Z4 and Z5 are two trinucleotides which code for any two amino acids, Z6 is a trinucleotide which codes for Leu and Z7 is a nucleotide. Please see attached alignment of OZ and Kasparkova's sequence of Figure 1.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally A Sakelaris whose telephone number is 571-272-0748. The examiner can normally be reached on M-Fri, 9-6:30 1st Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sally Sakelaris

8/11/2004

JEFFREY FREDMAN
PRIMARY EXAMINER
8/13/04